

REMARKS

STATUS OF THE CLAIMS

Claims 1-10, 24-40, 42-43, 49-60, 63-75 were pending. As shown above, claims have been amended to indicate that the claimed polynucleotides encode an HIV polypeptide, which polypeptide elicits a *Gag*-specific immune response (*see*, claims 2, 4, 5 and 6). In other words, the characteristics and/or functions of an HIV *Gag* polypeptide are no longer at issue. As noted by the Examiner, the specification teaches that sequences encoding polypeptides that do not exhibit non-immunogenic "*Gag*" functions are included within the scope of the claims, so long as the polypeptides elicit a *Gag*-specific immune response. *See, e.g.*, Example 4 of the specification. Claims 1, 3 and 67 have been canceled, without prejudice or disclaimer. The dependencies of claims 7, 8, 9, 24, 26, 27, 41, 74 and 75 have also been amended to properly depend from claim 2 and/or claim 4. The amendments are made to expedite prosecution and are not made for reasons related to patentability. Thus, claims 2, 4-10, 24-40, 42-43, 49-60, 63-66, and 68-75 are pending as shown above.

SPECIFICATION

Applicants have amended the specification to remove embedded hyperlinks as requested by the Office.

In addition, Applicants have inserted the appropriate sequence identifier on page 70 of the specification. The Sequence Listing including SEQ ID NO:30 was previously submitted to the U.S. Patent and Trademark Office on August 26, 2003.

FUNCTIONAL LANGUAGE

In the Office Action, it was maintained that the claims still read on polypeptides having the functional characteristics of a wild-type HIV *Gag* polypeptide (*e.g.*, virus assembly, virion manufacture, early post-entry step in virus replication, etc.). *See, e.g.*, pages 4, 8, 10, and 13 of the Final Office Action.

The foregoing amendments obviate this concern, inasmuch as the claims do not read on sequences that necessarily encode a "*Gag*" polypeptide, but rather, encompass sequences that encode any polypeptide that elicits a *Gag*-specific immune response. In other words, the claims no longer read on sequences encoding a *Gag* polypeptide, with all the various functions intrinsic to *Gag* polypeptides. Thus, as discussed during the telephone interview held on October 5, 2004, the foregoing amendments render moot the Examiner's primary concerns about the functions of the polypeptides encoded by the claimed sequences.

INTERVIEW

Applicants thank Examiner Whiteman for taking the time to talk with the undersigned and Dr. Michael Moran by telephone on Tuesday, October 5, 2004 regarding the remaining issues under 35 U.S.C. § 112, first paragraph (enablement and description), primarily in the CIP of this case (USSN 09/610,313), which has similar claims relating to polypeptides that elicit a *Pol*-specific immune response. Applicants address the issues regarding 112, first paragraph, set forth in the Office Action, and discussed by telephone (primarily in the companion case), below.

35 U.S.C. § 112, FIRST PARAGRAPH, ENABLEMENT AND DESCRIPTION

A. INOPERATIVE EMBODIMENTS

In the instant Office Action and during the telephone conference, the Examiner reiterated that there may be polynucleotide sequences falling within the 90% identity requirement that do not encode an immunogenic polypeptide and, accordingly, that it would require undue experimentation to determine operative species, other than those disclosed in the specification.

Applicants reiterate that the presence of inoperative embodiments does not necessarily render a claim nonenabled. *See, e.g.*, MPEP § 2164.08(b); and *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219, CCPA 1976. The test of enablement is not what is predictable *a priori*, but what the specification teaches the skilled practitioner in regard to the claimed subject matter. Thus, not every species (or even a majority of species) encompassed by the claims, even in an unpredictable area like the chemical sciences, needs to be disclosed. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219, CCPA 1976. The notion that one of ordinary skill in the art must have reasonable assurances of obtaining positive results on every occasion has been emphatically rejected. *Angstadt* at 219. So long as it is clear that some species render the claims operative, the inclusion of possible inoperative species cannot invalidate the claim under paragraph 1 of 35 U.S.C. §112. *See, also*, *In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, CCPA 1971; *Horton v. Stevens*, 7 USPQ2d 1245, 1247, Fed. Cir. 1988.

In the pending case, Applicants again note that every single nucleotide species exhibiting 90% identity to SEQ ID NOs: 3 and 4 can be determined *a priori* and, as such, the entire genus of polynucleotides exhibiting 90% identity to these sequences is enabled by the specification as filed.¹ Likewise, the polypeptide encoded by each and every one of these sequences can also be

¹ Applicants also direct the Examiner's attention to Example N:DNA of the Patent Office's "Training Materials for Examining Patent Applications with respect to 35 U.S.C. § 112, First Paragraph -- Enablement -- Chemical/Biotechnical Applications," which states that even with a very large genus of sequences (at least 1.26×10^{21}), undue experimentation is not required to determine all members of the genus because "each embodiment can be readily identified using the genetic code, synthesized using conventional methods, and used in the manner taught in the specification." see, page N-4.

determined *a priori*. Thus, there are no inoperative "structural" embodiments encompassed by the claims and, as such, the specification clearly enables the structures (sequences) of the claims.

Moreover, as set forth in the case law described above, the possibility that there may be some inoperative "functional" embodiments (e.g., some of the polypeptides may not elicit a *Gag*-specific immune response) does not render the specification nonenabling because the specification clearly teaches how to test for immunogenicity and indicates that such testing is utterly routine. *See, e.g.*, Declarations of Record. Routine experimentation, as would be required to determine if an embodiment falls within the "functional" scope of the claims, is not undue experimentation.²

Thus, not only does the claim language itself exclude inoperative embodiments, namely any and all nucleotide sequences that encode polypeptides that do not elicit *Gag*-specific immune responses, the experimentation needed to identify inoperative embodiments is not undue. Accordingly, the presence of potentially inoperative functional embodiments cannot form grounds for rejecting the pending claims as allegedly nonenabled.

B. STRUCTURE:FUNCTION CORRELATION

During the telephone conference, Examiner Whiteman also indicated that the specification is not enabling because it does not set adequately set forth a correlation between the structure of the polypeptide encoded by the claimed sequences and the functions of these polypeptides, for example by not enumerating "essential" nucleotides that are required in order to encode an immunogenic polypeptide.

As Applicants noted during the telephone conference, the correlation between polypeptide structure (primary sequence or tertiary structure) and immunogenic function can tolerate many modifications. In other words, whereas essential residues are readily identifiable for enzymatic (e.g., catalytic) functions, any polypeptide can tolerate multiple substitutions at various residues while still retaining its immunogenic function.³ This is also set forth in Dr. Ullmer's Declaration of record, for example in paragraph 18.

Indeed, as noted above, the claims no longer encompass sequences encoding a polypeptide having non-immunogenic (e.g., enzymatic or catalytic) functions of a *Gag* polypeptide. Thus, this concern is obviated by the foregoing amendments.

² *See, also, United States v. Telectronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989)), holding that routine experimentation, even if extensive (on the order of six or more months and tens of thousands of dollars), is not necessarily undue.

³ Nor does immunogenic function necessarily depend on tertiary structure. Simply put, wild type folding is not critical to generating an immune response and, accordingly, the references cited on page 14 of the Final Office Action are not relevant to the enablement or description inquiry.

C. THE SPECIFICATION DESCRIBES CLAIMED IMMUNOGENIC FUNCTION

Written description, particularly as it relates to the recited immunogenic function, was also discussed during the telephone conference. In this regard, Examiner Whiteman invited Applicants to present a copy of relevant PowerPoint slides presented by Christopher Low at the BioScience Forum on Thursday, September 9, 2004. (Appendix A, attached hereto).

In this presentation, Examiner Low indicated that a claim essentially identical to independent claim 1 as presented herein satisfied the written description requirement because the specification set forth "sufficient support" that the protein encoded by the claimed genus of polynucleotides had a specific, substantial, and credible use related to the claimed activity ("activity X"). *See, e.g.*, slide #17 of Examiner's Low presentation, where the exemplary claim reads:

An isolated and purified nucleic acid comprising a nucleotide sequence that is 90% identical to SEQ ID NO:1, wherein said nucleic acid encodes a protein having activity X.

Indeed, the exemplary claim presented in Examiner Low's presentation is the polynucleotide equivalent of the claim presented in Example 14 of the PTO's "Synopsis of Application of Written Description Guidelines." Both of these exemplary claims are considered adequately described in view of a specification that discloses examples of sequences having the claimed activity and methods of determining the presence or absence of such activity.⁴

Thus, like Examiner Low's example and like Example 14, the specification as filed provides sufficient support demonstrating that the protein has a specific, substantial and credible use related to immunogenicity. Thus, the written description requirement is satisfied.

Applicants also note that in the Advisory Action mailed in the CIP of this case, Examiner Whiteman did not consider this evidence, alleging that there was not "good and sufficient reasons" given as to why the evidence had not previously been presented. Examiner Low's talk was given in September of this year and discussed during a telephone interview only several weeks later. Thus, this evidence was not previously presented because it was not previously available.

⁴ In addition, Applicants note again how their description of particular sequences and recitation of these sequences in the claims distinguishes the pending case from *University of California v. Eli Lilly*. In *Eli Lilly*, the claims failed to recite any reference sequence whatsoever and, therefore, the genus encompassed by the claims included any polynucleotide encoding insulin. In contrast, the genus encompassed by the pending claims is fully described because every sequence exhibiting 90% identity can be envisioned from the reference sequences.

D. FURTHER EVIDENCE OF ENABLEMENT AND ADEQUATE DESCRIPTION

Applicants also submit herewith further evidence establishing the patentability of the claims as pending. In particular, Applicants direct the Examiner's attention to U.S. Patent No. 6,602,705, an issued patent with claims and disclosure highly analogous to those in the pending case, the difference being that U.S. Patent No. 6,602,705 claims polynucleotide sequences derived from subtype B sequences while the pending application claims sequences derived from subtype C sequences. Indeed, the guidance provided by this issued Patent regarding percent homology and assaying immunogenicity is virtually identical to that provided in the pending specification. Thus, U.S. Patent No. 6,602,705, an issued and presumptively valid U.S. Patent, provides still further evidence that the Patent Office considers claims such as those pending herein to be adequately described and fully enabled.

35 U.S.C. § 112, SECOND PARAGRAPH

Claim 26 was rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. (Office Action, page 29). In particular, it was noted that there was insufficient antecedent basis for the recitation "transcriptional promoter."

Applicants have amended claim 26 as shown above to depend from claim 25 instead of claim 24. Accordingly, there is sufficient antecedent basis for the term "transcriptional promoter" and withdrawal of this rejection is respectfully requested.

35 U.S.C. § 102(f)

Claims 3, 8, 9, 10, 24-40, 67 and 74 were rejected under 35 U.S.C. § 102(f) as allegedly not invented by Applicant but disclosed in U.S. Patent No. 6,602,705, which was cited for claiming sequences exhibiting 90% identity to SEQ ID NO:2 of the instant application. (Office Action, page 30). Claims 1-4, 67, 68, 69 and 74-75 were similarly rejected over co-pending application 09/899,575, which was cited for disclosing sequences identical to SEQ ID NOs:1 and 2 in the pending application. In addition, claims 1-6, 24, 27, 41, 42, 43, 67-74 were also rejected over co-pending application 09/967,464, which was cited for claiming sequences exhibiting 99-100% identity to SEQ ID NOs:1-4 of the pending application.

With regard to U.S. Patent No. 6,602,705, Applicants note that cancellation of claims directed to SEQ ID NO:2 obviates these rejections.

Turning to USSN 09/967,464 and USSN 09/899,575, Applicant notes that these applications are both later-filed applications and, therefore, are not available as references.

Furthermore, these applications contain additional claims that are not presently pending in the instant case and, hence, additional inventors are present on these later-filed applications.

DOUBLE PATENTING

Claims 1-4, 67, 68, 69, 74 and 75 were provisionally rejected under the judicially created doctrine of obviousness type double patenting as allegedly obvious over claims 7, 8 and 16 of co-pending application 09/899,575. In addition, the same claims were also alleged to not be patentably distinct from claims 7, 8 and 16 of co-pending application 09/899,575. Applicants note that the pending application is the grandparent application of 09/899,575 and, accordingly, the rejection should be withdrawn in this case and, if appropriate, applied in co-pending application 09/899,575.

Claims 1-6, 24, 27, 41, 42, 43 and 67-74 were provisionally rejected under the judicially created doctrine of obviousness type double patenting as allegedly obvious over claims 7, 26, 28, 31-50 and 72 of co-pending and commonly owned application 09/967,464. In addition, the same claims were also alleged to not be patentably distinct from certain unidentified claims of co-pending application 09/967,464. Applicants note that 09/967,464 is later filed and, therefore, is not available as a reference. Accordingly, the rejection should be withdrawn.

Finally, claims 3, 8, 9, 10, 24-40, 67 and 74 were provisionally rejected as allegedly obvious over claims 1-5 and 10-30 of U.S. Patent No. 6,602,705. Claims 1, 3, 67 and 74-75 were alleged not be patentably distinct from claims 1-5 and 10-30 of U.S. Patent No. 6,602,705. Applicants note that the foregoing amendments to the claims obviate these rejections and request that the rejections based on U.S. Patent No. 6,602,705 be withdrawn.

CONCLUSION

In view of the foregoing amendments, Applicants submit that the claims are now in condition for allowance and request early notification to that effect.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §1.16, §1.17, and §1.21, which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648, referencing Atty. Docket No. 2302-1631.20.

Please direct all further written communications regarding this application to:

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Date: February 17, 2005

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